prosecute the non-elected subject matter in subsequent divisional application pursuant to 35 USC 121.

Newly Added Claim

Claim 69 has been added, and covers the use of the combination of medroxyprogesterone acetate at a dosage of about 1.5 mg and conjugated estrogens, USP at a dosage of about 0.45 mg for the treatment or inhibition of vasomotor symptoms. Basis for this claim is provided in the tables on page 9 of the specification, and in Figures 1 and 2 of the application. This claim is clearly covered by the elected subject matter, and it is requested that this claim be examined with the elected subject matter. No new or additional examination is necessary because of the addition of this claim.

Rejection under 35 USC 103

Claims 7-14 stand rejected under 35 USC 103 as being obvious over Plunkett [US 4,826,831, Re 36,247; references to this document (including column and line numbers) in this response will be made using Re 36,247]. For the reasons provided below, the applicants respectfully traverse this rejection and request reconsideration.

The overriding law in determining whether a claimed invention is obvious over the prior art requires that an analysis must be undertaken based on several factual inquiries which include: "(1) the scope and content of the prior art; (2) the difference between the prior art and the claims at issue; (3) the level of ordinary skill in the art at the time the invention was made; and objective evidence of nonobviousness, if any." In re O'Farrell 7 U.S.P.Q.2d 1673, 1680 (1988) (citing Graham v. John Deere Co. 383 U.S. 1, 17-18 (1966)). An analysis of the prior art in relation to the claimed invention is provided below.

Applicant's Claims 7-14 cover a method of treating or inhibiting vasomotor symptoms comprising providing the continuous administration (28 days per 28-day cycle) of a combination of conjugated estrogens, and a daily dosage of about 1.5 mg of medroxyprogesterone acetate (Claim 7). Dependent claims provide dosage ranges of between about 0.625 and about 0.3 mg conjugated estrogens (Claim 9); between about 0.45 and about 0.3 mg conjugated estrogens (Claim 10), and about

0.3 mg conjugated estrogens (Claim 11). New claim 69 covers a dosage of about 0.45 mg conjugated estrogens. Claims 12 and 14 cover hot flushes specifically.

Claims 7-14 stand rejected as being obvious over US Re 36,247 (hereinafter referred to as Plunkett). Plunkett discloses a method of hormone treatment for menopausal or postmenopausal disorders by the continuous administration of estrogen and progestin combinations. Such treatment is commonly referred to as hormone replacement therapy (HRT).

It is well established case law that the prior art must be considered for everything it teaches, and not just specific aspects that it describes. The teaching of the prior art as a whole must be considered. (See, *EWP Corp v. Reliance Universal, Inc.,* 225 USPQ 20.) "A reference must be considered not only for what it expressly teaches, but also for what it fairly suggests." (*In re Burckel*, 201 USPQ 67). Plunkett discloses a plethora of estrogens and progestins that can be combined to treat numerous disorders. The estrogens disclosed are provided in Table 1A. Specifically the following twenty estrogens are described as being useful in the estrogen plus progestin combination for treating menopausal or post menopausal disorders: estradiol, estradiol-17β, estradiol valerate, conjugated equine estrogens, estrene, piperazine estrone sulfate, estriol, estriol succinate, polyestriol phosphate, ethinyl estradiol, mestranol, quinestrol, stilbestrol, stilbestrol dipropionate, diethylstilbestrol, chlorotrianiscos, benzoestrol, hexoestrol, and methallenostril.

Table 1B specifically discloses seventeen progestins to choose that are useful in the continuous HRT regimens: levo-norgestrel, dl-norgestrel, norethindrone, norethindrone acetate, dydrogesterone, medroxyprogesterone acetate, norethynodrel, allylestrenol, lynoestrenol, quingestanol, medrogestone, norgestrienone, dimentisterone, ethisterone, cyproterone acetate, chlormadinone acetate, and megestrol acetate.

Plunkett also provides ranges of dosage minimums and maximums, and preferred dosages for the estrogens and progestins listed. In the tables for conjugated equine estrogens, Plunkett lists the minimum dosage as 0.3 mg, the maximum dosage as 2.5 mg, and 0.6 mg as the preferred dosage. For

medroxyprogesterone acetate, Plunkett provides the minimum dosage as 1 mg, the maximum dosage as 15 mg, and the preferred dosage as 2.5 mg.

Column 6, line 46 of Plunkett further provides "Any of the suitable estrogens and progestogens (particularly those listed in the foregoing tables) may be combined with one another in the quantities recited to give estrogen/progestogen combinations within the purview of the invention."

From reading Plunkett, one skilled in the art could choose from many thousands of different combinations of estrogens and progestins that are useful in treating HRT, all at varying dosage ranges.

Plunkett also provides a list of twenty "especially preferred" combinations which include (see column 6, line 53): estradiol/levonorgestrel; estradiol 17β/levonorgestrel; estradiol valerate/levonorgestrel; conjugated equine estrogens/levonorgestrel; estradiol/dl norgestrel; estradiol 17β/dl norgestrel; estradiol valerate/dl norgestrel; conjugated equine estrogens/dl norgestrel; estradiol/norethindrone; estradiol 17β/norethindrone; estradiol valerate norethindrone; conjugated equine estrogens/norethindrone; estradiol/norethindrone acetate; estradiol 17β/notethindrone acetate; estradiol valerate/norethindrone acetate; conjugated equine estrogens/norethindrone acetate; estradiol/medroxyprogesterone acetate; estradiol 17β/ medroxyprogesterone acetate; estradiol valerate/ medroxyprogesterone acetate; and conjugated equine estrogens/ medroxyprogesterone acetate.

Of these thousands of possible combinations of estrogens and progestins, Plunkett only provides data for a single combination in which a study was conducted using a regimen of 1 mg/day 17β-estradiol plus 75 μg/day dl norgestrel. No data were provided for any combinations of conjugated estrogens plus medroxyprogesterone acetate.

Applicant's claimed subject matter represents a narrow species within the extremely broad genus of estrogens and progestins disclosed by Plunkett. It is well established that a species is patentable within a prior art genus absent teaching that

would motivate one skilled in the art to make the applicant's invention. In a case similar to the applicant's, the court in *In re Baird* held that a genus of a patent covering an estimated 100 million compounds did not render obvious a species that was encompassed by the genus, where there was nothing in the patent that does not describe or suggest the species itself, and therefore does not motivate its selection. (29 USPQ2d 1550). Similarly, the court in *In re Jones* held that the claimed novel (aminoethoxy)ethanol salt of dicamba cannot be held to be prima facie obvious in view of a prior art patent which disclosed dicamba in free acid, ester, and salt forms. (21 USPQ2d 1941).

As applied to the instant case, applicant's claimed invention is a species covered by Plunkett that is not specifically taught or suggested. As discussed above, Plunkett discloses a multitude of estrogen plus progestin combinations, all at different dosage ranges. Even the preferred combinations number 20, and all at different dosage ranges. The working example given did not exemplify the components of the applicant's combination, but rather exemplified 17β estradiol plus dl norgestrel. The applicants submit that there if no motivation provided within Plunkett to choose their specific combination. The disclosure is huge, the working example does not teach or suggest the use of a combination of conjugated estrogens plus medroxyprogesterone acetate, the applicant's dosages are significantly lower than the preferred dosages in Plunkett's tables.

All of the applicant's claims require a dosage of about 1.5 mg of medroxyprogesterone acetate. This dosage is sixty-six percent below the preferred dosage of medroxyprogesterone acetate provided in Table 1B of Plunkett (2.5 mg). With respect to applicant's Claims 10, 11, and 69, the dosage of conjugated estrogens (0.45 and 0.3 mg) is between thirty-three and one hundred percent lower than the preferred dosage of conjugated estrogens listed in Table 1A of Plunkett (0.6 mg). Accordingly, the applicants submit that there is nothing in Plunkett that would motivate the applicant to choose the specific combination of estrogen and progestin, at the specific dose range covered by the applicant's claims. Based on the broad disclosure in Plunkett, it would take undue experimentation for one skilled in the art to arrive at the applicant's claimed invention. At best, it would be obvious to try the applicant's claimed combination, however, it has long been held that obvious to try is

not a proper standard for rejection under 35 USC 103. Reconsideration is respectfully requested.

In summary, Claims 69 has been added, and the rejection of Claims 7-14 has been addressed. Accordingly, the applicants respectfully request reconsideration of the rejections, allowance of Claims 7-14 and 69, and passage of the case to issue.

Respectfully submitted,

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